CHAPTER VI: COMPLEMENTARY AND ALTERNATIVE MEDICINE AND AGING

Women's Aging Issues

Let's talk a little bit about women's health and estrogen. You'll recall this was a recent cover of *Time* magazine at the time of the publication of the Women's Health Initiative results. The population of women who live longer than men, women over 50, is going to double or triple over the next 3 decades. Importantly, women, healthy women, live about 3 decades after they've had a natural menopause. For those who have had an unnatural menopause at an earlier age, that's a different story. But normal aging in women has an average age of the transition (or menopause) at about 50. If you live to an average age of 80, it's obvious that you're spending 3 decades of life in this hormone-deficient state, at least from an ovarian steroid perspective. So what's the cost and impact of treating diseases that occur in women after they've undergone or sustained a normal menopausal transition as healthy women do? Well one thing, is that we think that this is going to continue to be an increasing problem of a major magnitude. So just some of the problems—I'm not going to spend too much time on this slide, and you'll see this more in the next couple—are cardiovascular disease, or CHD, cardiovascular heart disease, and stroke. The risk increases substantially after menopause. Whereas 1 in 50 women have this problem between 45 to 64 years of age, 1 in 3 women have serious cardiac disease after 65. That's a frightening change—more about that momentarily. Osteoporosis. You've all become sensitized to osteoporosis being a disease of aging in women. I might paramedically say that it's also an increasing disease in men. Dementia and Alzheimer's disease—we've talked about that a little bit. A variety of urinary tract dysfunctions that occur in women as they get older, including those listed problems with urination and so forth. But there are a lot of other conditions that affect women after menopause that become worse as they get older, including: cancer; lung disease; chronic obstructive pulmonary disease is a fancy way of saying emphysema; arthritis; diabetes; and depression. All of these conditions increase with advancing age.

Perception and reality are often a little different, and please pay attention to this in the next slide, because it's an important point here, really, I think. The leading cause of death among women in this country and in other western countries is heart disease—almost 1/2. Breast cancer, you'll notice, is 4%, other cancers 10% to 15%, and then the all-encompassing "other." But keep in mind that these are the objective facts. Most women die of heart disease, not of breast cancer. Now what happens when you ask women what the leading causes of death are? Look at this slide. Quite different, isn't it? When they're asked, most women—these are well-educated women, women just like you—think that most women die of breast cancer; 39%. You saw 4% in the other figure, and only 18% or 20% die of heart disease. I just showed you it's 2½ times that—45%. So there's a disconnect here. We who try to communicate in the medical establishment have done a terrible job because there shouldn't be this disconnect if we're doing our jobs right. So I will not take the blame for the whole medical establishment; I'm not quite that magnanimous, but I will certainly say that we in the medical establishment have done a terrible job. Because we need to sensitize people to the reality of what's embedded in those slides to women.

Now the Women's Health Initiative, about which you've all heard a great deal, has several different components. We're not going to go over the different components. I just want to highlight a couple of points. In this particular element of the Women's Health Initiative, or WHI, 27,500 women who were postmenopausal were studied. In a very controlled fashion, they received either the 2 ovarian hormones estrogen plus progestin given as Premarin and Provera in combination—what's called Prempro, which is a combination of Premarin and Provera—or estrogen only in the form of Premarin. But they received the estrogen and progestin if they had a uterus in their bodies; if they did not have a uterus because they had a hysterectomy, they received only estrogen. The study began in 1991 and was anticipated to go on for 15 years. In other words, it's still just a few years away from its complete dénouement. But it was struck short. I think everyone in this room knows that it was stopped short to wide publicity, not the kind that you want to have, last July when it was found that there was a small but very significant—and when you multiply the numbers out times many people, it becomes

meaningful—increased risk of cardiovascular disease and heart attacks, strokes, blood clots, and breast cancer in those who received estrogen and progestin. This was information from those women who had a uterus in their bodies and were part of the study in which they received estrogen and progestin, Prempro, or a placebo. The arm of the study with women who had no uterus in their bodies has not been completed yet, and we don't know anything yet. But based upon that evidence, counterbalanced by a decrease in breakage of bones, what we call fractures, and a small decrease in the expression of colon cancer, which were outweighed by these more adverse consequences, this study was stopped. Stopping it was a very big deal as undoubtedly is known. Just last week in the *Journal of the American Medical Association*, there were data from this same exact study related to whether it would retard dementia or the loss of memory function. The results were disturbing. Not only did it not retard dementia, but actually it increased the risk of dementia and the combined risk of this increased dementia equaled the combined increased risk of all these things, which is really scary. So it's looking as if estrogen and progestin, which have been, I won't say a hallmark, but a standard or practice for many in western medicine for the last 3 decades, is not necessarily a good thing if your idea is to prevent cardiovascular disease, to prevent dementia, to prevent strokes, to prevent blood clots. We have better ways of treating osteoporosis, so we don't need these hormones. We may need these hormones more in the early phases of the menopausal transition for short periods of time, such as when women are having hot flashes and some transitional symptoms during that perimenopausal timeframe. It's unclear whether that's true yet, and that's an area, as I'll mention, that we need to study more.

So that, of course, puts a kibosh on the whole estrogen/progestin in many women's minds and also in their physicians' and health care providers' minds, which leads to CAM use in menopause, which is viewed as a natural extension or interest in nutrition, exercise, healthy lifestyles, behavioral things that you can do, nonpharmacologic interventions, to maintain or improve QOL, or quality of life, which we're all concerned about. As it happens, more than 30% of women use acupuncture or natural or plant-derived estrogenic or hormonal-like substances and/or herbal supplements. Most studies of

menopausal interventions, including those that are really well conducted in usually a few hundred people at a time, show that these estrogenic drugs, mainstream estrogenic drugs, have a good placebo effect**.** So what's the evidence? Well, the studies to date of these alternative or CAM modalities have been really small and not always well done. They indicated that some products may relieve some symptoms, but the studies are too small to really make much sense of them.

The basic studies, that is the laboratory-based studies, have identified various agents, which are either part of these extracts or purified components, that may observe beneficial effects in the laboratory sense, but it's by no means clear that translated to giving them to people would be good or safe. No studies have really been conducted yet to determine whether these products are effective or safer than the mainstream hormones.

In the next couple of slides, I'm just going to quickly flash through and not talk about specifically, is a list of things , by no means all inclusive, that many women use in their attempts to allay hot flashes, which are commonest during this perimenopausal transition but can occur throughout the last cycle of both older women, including in advanced age. Sometimes women in their 70s, 80s, and even beyond have hot flashes. Sometimes they have them recur or even appear for the first time. There are reasons for that, which I won't discuss. But these things that are listed here are thought by most of us who really are studying them to not be terribly effective. The things that are listed here are thought to be kind of intermediate. Again, all of this needs much more research. The things that are listed here include SSRIs, which is shorthand for the most common class of medicines used as an antidepressant. As it happens, antidepressants, because of the way they work, are very helpful in some women with hot flashes and some of these other things. But they all need more studying.

Phytoestrogens are really a hot topic. They come in a variety of flavors so to speak. I want to talk a little bit about plant estrogens and phytoestrogens. First, there are very limited cross-cultural, that is, between country, studies, but they do suggest that the incidence of cancer and heart disease or atherosclerosis may decrease with increasing

dietary intake of some of these related products, which we'll refer to as bioflavonoids. But we believe, based upon epidemiological studies, which are studies of populations rather than studies where we give things to people, that these protective effects tend to occur over a lifetime. It isn't really known whether changing the diet in middle-age, because suddenly the clock has struck 50 years, is really a useful thing to do. In addition, no single synthetic or chemical derived from these soy products matches eating them in the diet. Just today in a corner of the *Washington Post*, in a health corner of the daily paper, was a comment about a paper that I happen to be familiar with, from a particular person I happen to know, showing that in a very well-conducted study that the purified oral ingestion of these purified products derived from soy products was, in this particular setting as in so many others, useless. We believe that it's something about the mix, and we believe it's probably something about long-term ingestion. However, we don't know that for sure. So as the bottom line says, the effect of prolonged intake of dietary or super-dietary levels of these soy products is something that we really have to learn more about, because we are fumbling here.

I'm going to skip this and the next slide for the sake of time and focus on another question that is really of interest to many people, particularly women with breast cancer. Sad to say that breast cancer affects 1 out of 8 women in her lifetime, and I might say prostate cancer, as an equal opportunity employer, affects 1 out of 6 men in his lifetime. So these are discouragingly common conditions, and hardly a person in this audience exists, I think, who doesn't know someone close to her or him who has been so affected given the common nature of this. Because we've learned that estrogen is not good for breast cancer and it may contribute in some ways to its formation and propagation, we do things to counter the effects of estrogen. We get super-medicines and do things. What about the use of phytoestrogens, one of which is this substance called Genistein— does it prevent or promote cancer? Because when women have undergone typical therapy for breast cancer, they are rended in a state where their ovarian function and their estrogen production is usually eradicated. They, of course, may benefit from the treatment of their breast cancer, but they suffer in other ways from being estrogen deficient. Many of them turn to phytoestrogens because they believe it's weaker, it may help me, and it won't hurt

me. So what I want to say is that studies indicating the cancer-promoting effect of Genistein according to this authority should not be taken lightly. In other words, beware. In contrast, a review by another authority comes to an entirely opposite conclusion. "If women (with or without breast cancer) enjoy partaking of soy products, emphasis on 'with breast cancer,' then it seems quite reasonable for them to partake of them." This was based upon a major content expert in this field with a thorough review of the literature coming to the completely opposite conclusion. So, many women with breast cancer are treated with antiestrogen therapy, with a drug called tamoxifen, which you've all heard of I'm sure. The question is whether the women taking this drug, which wipes out their estrogen**,** should take these soy products. One particular article by a noted authority reviews this topic and says no. You get the sense that there is a lack of consensus here and a lack of consensus is predicated on a lack of good information.

What is NCCAM trying to do about this? Well listed here, I won't read them all, is a series of different projects that kind of derive from a number of things that I've said that need to be addressed. But in addition, we believe that a variety of partnerships need to be forged among government agencies, industry representatives, the academic community, and others—philanthropic and other organizations—to delineate more fully issues related to the quality of life surrounding the menopausal transition and beyond. Obviously we need to have better products. We've already said that several times. We also need to define what's in them better and conduct serious studies related to how much is right and how much is too much. In addition, we really need to do well-conducted clinical studies to determine, particularly in newly menopausal women, whether these may benefit the array of things that occur as women make that transition. It may not be good, as you've seen from the Women's Health Initiative, to give them things later on in life. We need to really pay attention to the large and sadly growing population, the sorority of women, who are breast cancer survivors. The good news is that they're surviving. That's the good news. The bad news is that there are all too many of them. This weekend is the Race for the Cure, as many of you who are affected by that know. We need large collaborative trials to study long-term activity and safety of these products. Obviously, we need to gain

more knowledge, and we need to transmit it effectively to each other so those disconnects that you saw won't be disconnects any further.